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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/787,470	02/26/2004	Satoshi Takasaka	PC 26222A	9092

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EXAMINER	
CLAYTOR, DEIRDRE RENEE	
ART UNIT	**PAPER NUMBER**
1617	

DATE MAILED: 09/11/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/787,470	TAKASAKA, SATOSHI	
	Examiner	Art Unit	
	Renee Claytor	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Priority

This application claims priority to Japanese Application # 2003-053884 filed on 2/28/2003. Applicant's priority is acknowledged.

Claims 1-8 are pending and are being examined on the merits herein.

Specification

The disclosure is objected to because of the following informalities:

1. page 1, 5th line of last paragraph, the word "sometime" should be "sometimes".

2. page 2, 2nd line of the second paragraph reads "in days a at lower....", which should read "in days at a lower...".

3. page 4, 2nd line of the 4th paragraph and page 12, 1st line of the 5th paragraph reads "100nanomolar...." which should read "100 nanomolar....".

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 5 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant

regards as the invention. It is unclear as to whether the selectivity ratio is in comparison to other cGMP PDE receptors? What measurement is 100 referring to?

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 1-6 and 8 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for alleviating pain or spasticity in a patient suffering from spinal cord injury with sildenafil, does not reasonably provide enablement for alleviating pain or spasticity in a patient suffering from spinal cord injury with all cGMP PDE5 inhibitors. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7)

the presence or absence of working examples; and (8) the quantity of experimentation necessary.

(1) The Nature of the Invention: The rejected claim 1 is drawn to a method for alleviating pain or spasticity in a patient suffering from spinal cord injury comprising administration of a cGMP PDE5 inhibitor.

(2) The state of the prior art: The state of the art regarding treating spinal cord injury is relatively high (Hulsebosch, C.E., Recent advances in pathophysiology and treatment of spinal cord injury, 26: 238-255, 2002). However the state of the art for the treatment of spinal cord injury with all cGMP PDE5 inhibitors is underdeveloped. The skilled artisan would view that the treatment of spinal cord injury with all cGMP PDE5 inhibitors is highly unlikely.

(3) The relative skill of those in the art: The relative skill of those in the art is high.

(4) The predictability or unpredictability of the art: The skilled artisan would view that the treatment of spinal cord injury with all cGMP PDE5 inhibitors is totally, absolutely, or highly unpredictable.

(5) The breadth of the claims: Claim 1 embraces a method for alleviating pain or spasticity in a patient suffering from spinal cord injury comprising administration of a cGMP PDE5 inhibitor.

(6) The amount of guidance or direction presented: In the instant case, working examples are presented for treating spinal cord injury and spasticity with sildenafil in the specification on pages 17-19, studies were performed in patients with

spinal cord injuries in which the cGMP PDE5 inhibitor sildenafil was administered. As a result of the treatment, alleviation of pain or spasticity occurred in the patients tested proving that sildenafil was effective in alleviating pain and spasticity in patients with spinal cord injury. However, there are a lack of working examples presented in the specification as filed showing how to treat spinal cord injury with all cGMP PDE5 inhibitors. For example, the compound of formula (I) has many possible substitutions that can be applied to R^1, R^2, R^3, and R^4, thereby leading to distinct chemical compounds. Because each compound is distinct structurally, each compound may have different reactivity, solubility, oral bioavailability etc. In addition, not every cGMP PDE5 inhibitor has the same core structure of the compound of formula (I) (see for example Maw et al., U.S. Patent 6,586,439 for various forms of cGMP PDE5 inhibitors). Note that lack of a working example is a critical factor to be considered, especially in a case involving an unpredictable and undeveloped art. See MPEP § 2164.

(7) The presence or absence of working examples: Applicant provides working examples for alleviating pain or spasticity in a patient suffering from spinal cord injury with the cGMP PDE5 inhibitor sildenafil. However, applicant does not provide any working examples for alleviating pain or spasticity in a patient suffering from spinal cord injury with all cGMP PDE5 inhibitors.

(8) The quantitation of experimentation necessary: Claim 1 reads on a method for alleviating pain or spasticity in a patient suffering from spinal cord injury with a cGMP PDE5 inhibitor. As discussed above, the specification provides examples for alleviating pain or spasticity associated with spinal cord injury with the cGMP PDE5

inhibitor sildenafil, but the specification fails to provide sufficient support for alleviating pain or spasticity associated with spinal cord injury with other cGMP PDE5 inhibitors. As discussed above, cGMP PDE5 inhibitors have distinct structures, lending to different reactivity, solubility, oral bioavailability, etc. Applicant fails to provide information sufficient to practice the claimed invention, absent undue experimentation. Genetech, 108 F.3d at 1366 states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 1 and 7 rejected under 35 U.S.C. 103(a) as being unpatentable over Jain et al (Brain Research 909, 2001, 170-178) in view of Cardenas et al. (Arch Phys Med Rehabil Vol. 83, Dec. 2002).

Jain et al. teach that sildenafil is a cGMP PDE5 inhibitor that is useful in the treatment of pain (see in particular results and figures).

Jain et al. does not specifically teach that sildenafil or cGMP PDE5 inhibitors treat pain associated with spinal cord injury.

Cardenas et al. teach that chronic pain is associated with spinal cord injury (see whole document).

It is therefore obvious to one having ordinary skill in the art at the time the invention was made to combine the teachings of Jain et al., which teach that sildenafil is a cGMP PDE5 inhibitor and is useful in the treatment of pain, with Cardenas et al. which teach that pain is associated with spinal cord injury. One having ordinary skill in the art at the time the invention was made would be motivated to combine the teachings of Jain et al., with Cardenas et al. because the prior art teaches that sildenafil treats pain and spinal cord injury is associated with pain.

Claims 2-6 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jain et al. (Brain Research 909, 2001, 170-78) in view of Cardenas et al. (Arch Phys Med Rehabil, Vol. 83, Dec. 2002) as applied to claims 1 and 7 above, and in further view of Maw et al. (U.S. Patent 6,856,439).

Jain et al. and Cardenas et al. teach that sildenafil treats pain and that pain is associated with spinal cord injury.

Jain et al. and Cardenas et al. do not teach the route of administration, the dosage, the IC50, or the selectivity ratio of the cGMP PDE5 inhibitor.

Maw et al. teach a pharmaceutically active compound comprised of a cGMP PDE5 inhibitor that is used to treat various disorders, including female sexual pain disorder and sexual dysfunction due to spinal cord injury (Col. 25, lines 13-20). They further teach that the compound will be administered orally (encompassing claim 2, Col.

25, lines 52-53) and a dose range of tablets as being between 0.01 mg and 500 mg (encompassing claims 3 and 8; Col. 27, lines 30-31). It is also taught that the IC50 value is less than 100 nM (encompassing claim 4, Col. 40, lines 41-43).

Examiner assumes, for the sake of compact prosecution, that Applicant is referring to the selectivity ratio of cGMP PDE 5 inhibitors in excess of 100 to mean the selectivity ratio over other cGMP PDE receptors such as cGMP PDE 2, 3, and 4. The properties of the cGMP PDE5 inhibitor are inseparable; therefore, the cGMP PDE 5 inhibitor will have an identical selectivity ratio.

It is therefore obvious to one having ordinary skill in the art at the time the invention was made to combine the teachings of Jain et al., which teach that sildenafil is a cGMP PDE5 inhibitor and Cardenas et al. which teach that spinal cord injury is associated with pain, with the teachings of Maw et al. which teach a composition comprised of a cGMP PDE5 inhibitor to treat various disorders, including female sexual pain disorder and sexual dysfunction in patients suffering from spinal cord injury. One having ordinary skill in the art at the time the invention was made would be motivated to combine the teachings of Jain et al. and Cardenas et al. with Maw et al. to obtain an efficacious compound to alleviate pain associated with spinal cord injury.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Renee Claytor whose telephone number is 571-272-8394. The examiner can normally be reached on M-F 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Renee Claytor

SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER